REMARKS

Claims 1-14, 16, and 20-35 remain in the application. Claims 1, 16, and 30 are in independent form.

Applicants wish to express their appreciation for the courtesies extended Applicants' representatives, Gregory E. Stanton and Dr. Kenneth I Kohn, during a telephone conference in which the outstanding Office Action was discussed. Further to the discussion, claims have been amended to stress the ability of the claimed invention to capture retinal fluorescence images ***immediately*** after exposure to excitation illumination.

Applicants have amended the claims to more precisely claim the present invention and distinguish the claimed invention over the applied art. Independent claim 1, as amended, claims a device for measuring apoptotic activity of an eye (support in detailed description paragraph 14, lines 9 *et seq.*) The device includes an excitation light source for providing excitation light at a wavelength corresponding to the excitation of flavoprotein auto-fluorescence. The device further includes image capture means for recording a single image representative of a retinal fluorescence signal generated immediately in response to the excitation light. This capability eliminates the need for long exposure times and repeated image acquisitions required by the references applied by the final Office Action. This capability minimizes or eliminates inaccuracies introduced by eye movements and rapid physiological changes such as blood vessel pulsation. This capability arises from an image intensifier means for providing a focused amplified image showing evidence of apoptotic activity in the eye.

The term "immediately" is supported in the Background (paragraph 7), in which it is recognized that there is a need for a "device and method…that increases…diagnostic accuracy and speed…"; in the Summary (paragraph 8): "Salient objectives …include…fast procedure time…"; and in the Detailed Description (paragraph 20), "…integration time (is) typically less than one second".

Claims 16 and 30 have been amended consistent with the present amendment of claim 1.

Specifically referring to the final Office Action, the independent claims were rejected under 35 U.S.C. §103 as being unpatentable over U.S. Patent 4,569,354 to Shapiro et al. (Shapiro) in view of U.S. Patent 6,478,424 to Grinvald et al. (Grinvald). Shapiro describes a device for determining oxygenation of the retina by scanning the retina, pixel by pixel, and measuring the fluorescence of flavoprotein in the retina independently at each pixel. In particular, a spot of excitation light is scanned across the retina spot-by-spot and line-by-line. As a result of this scanning process, the device of Shapiro takes some time to record fluorescence information for even a small portion of the retina. In other words, there is a significant time delay from the time at which fluorescence data from the first pixel is obtained until the time at which fluorescence data from the last pixel is obtained. Because of this time delay, eye movements and rapid physiological changes adversely affect the accuracy of the fluorescence information recorded by the Shapiro device. At least for this reason, Shapiro does not disclose or even suggest an "image capture means for recording a single image representative of a retinal fluorescence signal generated ***immediately*** in response to the excitation light ***to minimize inaccuracies introduced by eye movements and rapid physiological changes***" as now recited in claim 1.

Grinvald also does not disclose or suggest an "image capture means for recording a single image representative of a retinal fluorescence signal generated immediately in response to the excitation light recorded ***to minimize inaccuracies introduced by eye movements and rapid physiological changes***" as now recited in claim 1. Grinvald describes a technique in which multiple images of an eye are captured: one or more baseline images, in which the eye is "at rest" (i.e., the eye has not been stimulated by visible light), and one or more response images taken during stimulation or after stimulation of the eye with visible light. The baseline images measure reflectance or fluorescence of the eye at rest, and the response images measure reflectance or fluorescence of the eye after or during stimulation by visible light. (*See Grinvald* at col. 3, lines 12-26, 53-56; col. 4, lines 56-61.) The delay between the taking of the first image and the taking of the last image may be several seconds. (*See Grinvald* at col. 4, lines 57-61; col. 6, lines 25-31).

Grinvald teaches that stimulation with visible light causes changes in the reflectance/fluorescence of the retina, and these changes can be measured by comparing the background and response images. Specifically, Grinvald explains that a differential image is generated based on the background and response images. Grinvald also explains that only the differential image provides any useful information regarding the retina's functional response to illumination:

> Other images acquired during or after stimulating retinal illumination are designated response images. Because of the small size of the functional signal, these response images look little different from the baseline images upon cursory examination. However, subsequent analysis reveals the small functional signal they contain ... Differential analysis now proceeds by one of two preferred methods. Either the single-condition blank image is subtracted from the single-condition response image, or the single-condition response image is divided by the single-condition blank image. Either of these mathematical operations, or one of others which may be trivially related, removes the unchanging background of the retinal reflectance/fluorescence image, leaving behind the functional response of the retina to visual stimulation. *Grinvald* at col. 7, lines 4-24.

Thus, in Grinvald, multiple images over several seconds must be taken in order to generate the differential image that reveals the functional response of the retina to visual stimulation. In other words, the differential image of Grinvald is not generated ***immediately and thus will not minimize inaccuracies introduced by eye movements and rapid physiological changes***. At least for these reasons, Grinvald also does not disclose or suggest an "image capture means for recording a single image representative of a retinal fluorescence signal generated ***immediately*** in response to the excitation light recorded ***to minimize inaccuracies introduced by eye movements and rapid physiological changes***" as now recited in claim 1.

At least for the reasons discussed above, both Shapiro and Grinvald, individually and in combination, fail to disclose or suggest all of the elements of claim 1. At least for this reason, the alleged combination of Shapiro and Grinvald does not render claim 1 unpatentable.

Additionally, if the combination of Shapiro and Grinvald asserted in the final Office Action were made, the alleged combination would be inoperable and/or would not include all of the elements of claim 1.

It appears that the Examiner is interpreting the photomultiplier tube of Shapiro as an image intensifier. As discussed above, in Shapiro a spot of illumination is scanned across the retina pixel-by-pixel and line-by-line. Thus, the photomultiplier of Shapiro processes light corresponding to only a single pixel, and is only capable of processing light corresponding to a single pixel. Grinvald, on the other hand, does not appear to disclose an image intensifier.

If Shapiro and Grinvald were combined as argued by the final Office Action, the alleged combination would fail to include an "image intensifier means for providing a focused amplified image showing evidence of apoptotic activity in the eye" as recited in claim 1. In particular, because the photomultiplier of Shapiro is only capable of processing a single pixel, it would not be able to process a fluorescence signal, such as generated in Grinvald, that corresponds to a 2-dimensional image of a retina. Thus, the photomultiplier of Shapiro cannot operate on a fluorescence signal that corresponds to a 2-dimensional image to provide an amplified ***image*** (e.g., a two dimensional array of pixels). In other words, the alleged combination of Shapiro and Grinvald would either be inoperable (because it could not function with the photomultiplier of Shapiro) or it would not include an "image intensifier means for providing a focused amplified image showing evidence of apoptotic activity in the eye" as recited in claim 1.

At least for this additional reason, the alleged combination of Shapiro and Grinvald does not render claim 1 unpatentable.

Applicants respectfully submit that independent claims 16 and 30, as amended, are allowable at least for reasons similar to those discussed above with respect to claim 1.

The remaining dependent claims are all ultimately dependent upon at least one of the independent claims discussed above. Applicants respectfully submit that the dependent claims are allowable at least for the same reasons as the independent claims from which they depend.

In view of the above, Applicants believe the pending application is in condition for allowance. This response is timely filed, as Applicants submit this response with a petition for a two-month extension of time, a Request for Continued Examination, and the appropriate fees. Although Applicants believe that no other fees or petitions are due, the Commissioner is hereby authorized to charge any fees or credit any overpayments to Deposit Account No. 13-2855 of Marshall, Gerstein & Borun, LLP under Order No. 30275/39376.

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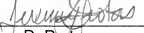
Respectfully submitted,

By 

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